Foreword

Concerns about health effects of low doses of radiation, including effects on radiation workers, patients, and the general population, stimulated much new research in the late 1940s and 1950s. Cancer was a principal concern. During that period, animal studies supported by various federal agencies were initiated or expanded at universities and newly created national laboratories; epidemiological studies on survivors at Hiroshima and Nagasaki were initiated; and results from studies of long-term survivors of radiation therapy received renewed attention.

Today, studies of the Japanese populations continue because nearly 50% of the exposed population still survives. Studies also continue on U.S radiation workers and various irradiated populations in states of the Former Soviet Union (FSU). Chronic radiation sickness characterized by pancytopenia and several other "soft" clinical signs have been reported among FSU persons who received doses of up to 1000 mSv over long periods at low dose rates. The FSU studies may yield important new data on human cancer risks with protracted doses as well as information on cellular repair capability in humans exposed at low dose rates.

Most of the animal research that focused on cancer induction and tissue injuries after single or protracted doses (at low dose rates) was completed or terminated before 1980 because of funding limitations and/or new research emphases that did not involve intact animals. Thus, the database on systemic responses and cancer in intact animals is more than 20 years old, and many of the data were collected at high doses and dose rates. For early effects in intact animals, low doses below 1000 to 2000 mSv have been largely neglected. Among the lessons learned from animal studies is that at low doses (at high or low dose rates) the definitive presence or absence of a "threshold" for cancer induction cannot be established. Also, hormesis, the induction of some degree of resistance to late effects by a low initial dose is likewise beyond the realm of rigorous statistical verification using animal models. Also, very large sample sizes, multiple replicates, and studies lasting many years are required for definitive low dose, animal-based studies in which cancer or prominent late-arising physiological changes are the major end points.

Because statistical uncertainties are very large when measured effects are either few in number or low in intensity, epidemiological studies on various large human populations are not likely to preclude or verify significant radiation effects at doses below 100 to 200 mSv. Where the concerns are human cancer, mortality, or heritable genetic changes, a linear nonthreshold model at low doses is accepted currently for risk estimation.

This conference concerned low-level radiation (LLR) where "low" was defined as 700 mSv (70 cGy) or below. Military personnel could be exposed over hours or days at high or low dose rates; various LLR exposure scenarios are possible. At doses of 500 to 700 mSv, early effects that could impact operations cannot be ruled out, but increased risk of cancer and heritable genetic damage are primary concerns. An important issue for the future is to explore means to mitigate radiation injury that could lead to these late effects. Several kinds of chemical agents that are now available reduce damage, stimulate repair, or modulate gene expression, and could confer some protection against any elevated cancer risk if a radiation exposure cannot be avoided. However, new research in this area is needed.

Where the issue is significant early injury to tissues or organs at 700 mSv or below, few relevant data are available at any dose rate. While it is generally accepted that a single brief dose of 500 mSv in humans can produce detectable marrow depression and possibly a transient decline in white blood count, the effects of low dose rates protracted over several hours or days are unknown. Marrow depression could reduce natural resistance to infection and increase susceptibility to biological warfare agents. Lacking, in any species, are systematic marrow injury studies in which the variables include total dose, dose rate, number of fractions or doses, radiation free time, and the total elapsed time. Using the endpoint of marrow depression as an example, determining the dose/dose rate/elapsed time relationships over a relevant dose range in several species would seem essential for model development concerning the consequences of combined injuries.

Combined injuries are an important issue. Specifically, what are the dose/dose rate combinations that increase susceptibility to infection whether it is pulmonary, intestinal, or from a wound? Is it clear that no effect would be expected at 700 mSv, a dose that, given at a high dose rate, would be expected to produce 40% to 50% killing of hematopoietic stem cells? The same kind of interaction concern could be expressed for chemical agents. For example, additional damage would be expected from whatever fraction of mustard compounds reaches the marrow from lung or skin contamination. At 700 mSv, are neurohumoral responses produced that could influence the central nervous system responses to chemical warfare agents alone or in combination with other chemicals that may be encountered on the battlefield?

Low dose/dose rate studies directly relevant to LLR issues are difficult. Most prior research on intact animals involved relatively high total radiation doses given at high or low dose rates because of ease in detecting responses. The possibility of radiation effects other than cancer at low doses is a major issue that requires careful consideration. In a military context, any possible mission-compromising debilitations need first attention, but any elevation of other long-term risks for veterans is also an issue. How does one proceed in dealing with these low dose issues? To conclude that it is not likely that a measurable effect occurs at a certain dose/dose rate combination probably requires data collection over a range of higher doses to establish the "threshold" for dose/dose rate combinations where effects are indeed produced. In this way, one could more confidently assert that significant injuries at lower doses and dose rates are not likely.

Finally, it is in the low dose/rate domain below 700 mSv where very important issues exist. Cancer risks to personnel and implementation of treatment strategies to reduce them are a priority. Mission accomplishment is the military goal, and identification of any early LLR radiation effects that could compromise goal attainment, such as increasing sensitivity to biological or chemical agents, are also of great concern. The application of novel approaches, models, and cellular and molecular methods to complement new studies on rodents and larger animals should produce the database needed to increase confidence in the prospect that missions would not be compromised by a dose of 700 mSv to military personnel. The essential database on experimental animals does not exist. Important issues remain to be addressed.

E. JOHN AINSWORTH, PhD
AFRRI Scientific Director, 1989-1998

Military Readiness Posture

Low-level radiation (LLR) as it relates to injuries and countermeasures is a serious challenge that faces our nation's military forces. It has tremendous political ramifications in this environment of negative tolerance for any injuries. It is imperative that research clearly and rapidly defines the medical effects of LLR exposure so that doctrine and policy can be developed to better protect our service members.

It was fitting that the Armed Forces Radiobiology Research Institute should host the LLR Conference, a gathering of experts from around the world. The Institute, chartered by the United States Congress in 1961, is a unique laboratory with multidisciplinary teams of radiobiologists, health physicists, microbiologists, and engineers. We recently added a new low-level cobalt-60 gamma irradiation facility to an already comprehensive array of radiation sources. The heavily shielded 1,600-square-foot walk-in facility will be used to study the potential health effects of chronic irradiation and the development of effective countermeasures.

We gratefully acknowledge the contributions of the conference participants and proudly present in this publication the ideas and concepts that were generated. We fully anticipate that greater understanding of and solutions to this health threat issue will be forthcoming.

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Preface

The LLR Conference Organizing Committee and the staff of the Armed Forces Radiobiology Research Institute invite your attention to the proceedings of the International Conference on Low-Level Radiation Injury and Medical Countermeasures. Low-level radiation, or LLR, is an area of growing concern due to potential threats to U.S. military personnel and operations. During the conference, we examined the LLR issue from a military perspective and attempted to better define methods by which to both assess and minimize the associated health hazards. For the purpose of this conference, the LLR exposure region was based on NATO and U.S. military radiological guidance documents that include radiation doses from background levels to as high as 700 mSv.

The National Academy of Sciences comprehensive report—"Potential Radiation Exposure in Military Operations: Protecting the Soldier Before, During and After," edited by S. Thaul, H. O'Maonaigh, and F.A. Mettler, Chairman, Committee on Battlefield Radiation Exposure Criteria, National Academy Press, Washington, DC, 1999—examines the LLR issue for military operations largely from a health physics perspective and includes legal and ethical issues. Our intention at the conference was to extend that information into assessment of injuries and development of preventive treatments.

The meeting had four major sessions: Session 1 on monitoring and assessments of LLR by physical and biodosimetric methods; Session 2 on preventive treatments; Session 3 on the effects of combined injury stemming from nuclear, biological, and chemical agent interactions; and Session 4 on developing consensus on assessment and treatment protocols. We also had a special session on the physiological and psychological impact of LLR on troop performance and function. In addition, two poster sessions provided an opportunity for conference participants to present their work on LLR issues.

We are pleased to present the results of the conference in this supplement.

THOMAS M. SEED, PhD
Conference Chairman